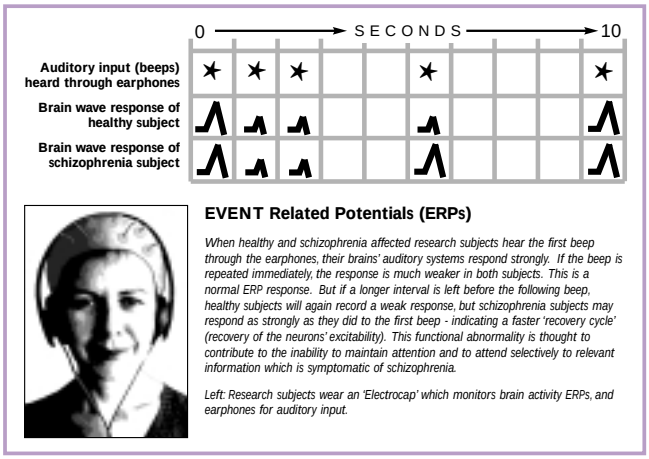
HEADLINES

The Newsletter of the Neuroscience Institute of Schizophrenia and Allied Disorders. March 2002.

Investigating the restless mind of schizophrenia

Australian Rotary's 'Ian Scott Research Fellowship' goes to Nathan Clunas and Schizophrenia Research.

Rotary Scholarship winner Nathan Clunas



EVENT Related Potentials (ERPs)

When healthy and schizophrenia affected research subjects hear the first beep through the earphones, their brains' auditory systems respond strongly. If the beep is repeated immediately, the response is much weaker in both subjects. This is a normal ERP response. But if a longer interval is left before the following beep, healthy subjects will again record a weak response, but schizophrenia subjects may respond as strongly as they did to the first beep - indicating a faster 'recovery cycle' (recovery of the neurons' excitability). This functional abnormality is thought to contribute to the inability to maintain attention and to attend selectively to relevant information which is symptomatic of schizophrenia.

Left: Research subjects wear an 'Electrocap' which monitors brain activity ERPs, and earphones for auditory input.

The Australian Rotary Health Research Fund Committee has awarded their Ian Scott Research Fellowship to Nathan Clunas, whose earlier research was assisted by a NISAD Grant-in-Aid. The Fellowship is worth $26,000 for 2002.

Nathan's research will investigate the brain function abnormalities which make some schizophrenia patients easily distracted, and unable to attend selectively to relevant information in their environment.

This tendency for 'scattered thoughts' may be due to a malfunction of the brain's inhibitory processes which modulate the excitability of neurons. Earlier studies have shown that neurons in schizophrenia brains are quicker to recover full excitability after firing.

Nathan Clunas' study will focus on the brain's auditory system because 'hearing voices' is one of the most common symptoms, indicating that the brain areas which process sound are particularly affected by the disease.

The research method used will be Event Related Potentials (ERPs) recorded via electrodes placed on the scalp. The brain areas responsible for generating auditory ERPs will then be investigated further using functional Magnetic Resonance Imaging (fMRI), and by comparing images from schizophrenia patients with bi-polar patients, and healthy subjects.

In this way, Nathan hopes to pinpoint the functional abnormalities specific to schizophrenia.

The research will be based at Liverpool Hospital's Schizophrenia Research Unit, which is directed by NISAD's Scientific Director Assoc. Professor Philip Ward.

Jackie Crossman

NISAD's New Executive Director

Six years ago, NISAD was little more than an idea in the minds of a few scientists and parents of children with schizophrenia. By 2001, the idea had developed into a statewide organisation recognised by government as the schizophrenia research institute of NSW.

Successful as this organisation has been during its establishment phase, NISAD's research capabilities and public profile still fall far short of the levels warranted by the prevalence of schizophrenia in the community. As a result, the Board has appointed Jackie Crossman as Executive Director to drive the development and implementation of a strategic plan aimed

Continued overleaf...

Voiceover: **"There are now more than 31,000 children in Australia who are expected to develop schizophrenia sometime after their 12th birthday. And this number is increasing with population growth".**

New TV Appeal for More Research Volunteers

The NISAD Schizophrenia Research Register is a unique database of patients who have made themselves available for research projects in NSW. Presently the Register lists around 500 members, which is a long way short of a number reflecting the prevalence of the illness. Consequently a new 30-second TV appeal has been produced, aimed at attracting a new batch of volunteers.

NISAD's Research Officer Jim Sheedy is now based at Westmead Hospital, and is interviewing Sydney Registrants. Newcastle-based Register Coordinator Carmel Loughland is also ready to sign-up more volunteers. So Marketing Director Alan Tunbridge has produced the video, and is now applying to all TV channels for free Community Service airtime.

The new TV appeal stresses the urgent need for more research by featuring portraits of babies and pre-teens representing the 31,000 Australian children who will certainly develop schizophrenia sometime after age 12 - if new preventative treatment is not discovered. This disturbing number is calculated from the 1% prevalence of the illness, and is increasing every day due to population growth.

A brochure and registration form for the NISAD Schizophrenia Research Register can be requested by calling 1800 639 295. Volunteers who do not have schizophrenia are also needed.

New Executive Director:

making NISAD better able to fulfil its mission.

Jackie brings to the role skills accumulated over 20 years of high level management in the marketing, communications and service industries. She was responsible for initiating and developing New Zealand's leading PR agency, and has won a number of global PR awards.

Her career has encompassed many campaigns for non-profit organisations such as Royal NZ Foundation for the Blind, Guide Dogs, RSPCA, and for health-related marketing efforts such as the New Zealand launch of a new antipsychotic medication.

Jackie has also had experience with major events from Sir Bob Geldof's Sport Aid in Australia, to New Zealand's successful defence of the America's Cup in 2000.

With such a record of achievement, the NISAD Board is confident that Jackie will develop and implement growth strategies for the future of schizophrenia research in NSW.

Trish Oakley Joins the Board

With her long experience as a high-level consultant to the government and corporate sectors, Trish Oakley brings a new dimension of know-how to the NISAD Board.

As a partner in her Brophy Oakley Consulting company, Trish handles media and management issues for government departments, and commercial organisations ranging from restaurant chains to pharmaceutical companies.

Following a distinguished career in TV journalism, Trish joined the staff of the then Deputy Leader of the Opposition, Dr Andrew Refshauge in 1990 as press secretary and political strategist. She played a critical role in two elections, including the election of the Carr Government in 1995. Upon gaining office, she was appointed Chief of Staff of the Deputy Premier's office and managed policy development and political strategy in the portfolios of Health, Urban Affairs and Planning, Housing and Aboriginal Affairs.

Trish has a degree in Law and a Bachelor of Arts in Government. She undertakes pro-bono work for Assistance Dogs for Independence, as well as NISAD.

Attracting the Brightest Brains

A vital part of NISAD's mission is to promote schizophrenia research as a bright career choice to young scientists.

NISAD PhD Scholars (Clockwise from top left) Karin Aubrey, Kelly Newell, Judith Weidenhofer and David Wheeler.

Since the World Health Organisation's 1993 report 'The Global Burden of Disease' established the true prevalence and financial cost of mental illnesses, national authorities have assigned higher priority ratings for mental health programs. In turn, the hitherto low-profile field of brain research has burgeoned - attracting increasing numbers of young scientists to consider it as their career discipline.

Initiated in 1998, NISAD's Summer Student Scholarships program has aimed at channelling this new wave of interest by providing opportunities for young scientists to enter the field of schizophrenia research. To date, the Institute has supported 14 Summer Scholars at its Centres for Collaborative Human Brain Research at the Universities of Sydney, Newcastle and Wollongong. From December 2001, undergraduates Wayne Anderson, Sinthu Sithamparanathan and Tu Hao Tran have gained experience in tissue-based schizophrenia research during their 6 to 8 week scholarships at NISAD Centres.

Happily fulfilling the aim of this program, Ms Kelly Newell, a Summer Scholar of 2000, has returned after completing her tertiary degree, and has been awarded a NISAD PhD Scholarship for neurobiological schizophrenia research.

NISAD Launches PhD Scholarships

Four young scientists have been awarded inaugural NISAD PhD Scholarships in neurobiological schizophrenia research.

Karin Aubrey continues her PhD project investigating the role glycine transporters play in neurotransmission - with a view to developing a new pharmacological treatment for schizophrenia. *PhD Project Title: Regulation and modulation of glycine transporters.*

Kelly Newell will investigate how schizophrenia affects neurotransmitter receptor systems in the posterior cingulate cortex brain region, particularly any neuronal damage caused by the illness, and to what degree this damage may be prevented by the use of antipsychotics such as haloperidol, clozapine and olanzapine. *PhD Project Title: Neural Pathophysiology of Posterior Cingulate Cortex in Schizophrenia.*

David Wheeler will investigate possible neurobiological abnormalities affecting memory function by comparing post-mortem brain tissue from individuals diagnosed with schizophrenia, Alzheimer's, and alcoholic Wernick-Korsakoff syndrome with tissue from individuals with no history of psychosis. *PhD Project Title: Memory dysfunction in schizophrenia, Alzheimer's disease and alcoholic Wernicke-Korsakoff's syndrome .*

Judith Weidenhofer aims to expand our knowledge of the role of tachykinin neurotransmitters and their receptors in schizophrenia, and to determine if the illness alters gene expression profiles, particularly those of tachykinins. *PhD Project Title: The role of the tachykinins and their receptors in schizophrenia: An investigation at a cellular and genetic level.*

Newcastle Scientists Win More Support for Schizophrenia Neuroimaging

Scarcely 10 years old, functional Magnetic Resonance Imaging (fMRI) is one of the new neuroscience tools now being used to investigate the abnormal brain functions behind the symptoms of mental illnesses. As part of NISAD's commitment to increase fMRI schizophrenia research in NSW, the Institute funded the neuroimaging analysis system used at the Centre for Mental Health Studies at University of Newcastle, and collaborated with the Centre's researchers on several key studies. Lead by NISAD Director Prof. Pat Michie, and NISAD Neuroimaging Panel member Dr. Ulrich Schall, the Newcastle teams have now obtained funding from the Clinical Neuroscience Program of the Hunter Medical Research Institute for a Research Lecturer position. The appointee will make a vital improvement to the team's capacity to process the fMRI data to be collected for such studies as, *Facial recognition in schizophrenia and healthy subjects*, and *Effects of THC (Cannabis) use on cognitive performance in substance users and co-morbid schizophrenia patients.*

Lisa Azizi

Lisa Azizi Joins the 'Gift of Hope' donor program

The NISAD "Gift of Hope' Tissue Donor Program was officially launched in October 1999. However, the program's Coordinator Margaret Boyes had already worked long and hard to gain approvals from ethics committees on registration and collection procedures, and to coordinate the collection process itself. The Program has now signed-up around 25 donors, with a further 80 waiting to be interviewed. NISAD's new Research Assistant Lisa Azizi is now based at the NSW Tissue Resource Centre at the University of Sydney, working with Margaret Boyes on the donor interviews which will make 'Gift of Hope' donations so valuable to future researchers. Lisa also works with the NSW Tissue Resource Centre, focussing on the collection and classification of donated tissue.

SCHIZOPHRENIA 2002 CONFERENCE SET FOR BONDI IN OCTOBER

Convened by NISAD Founding Chairman Stan Catts, the Australasian conference 'Schizophrenia 2002' will invite speakers representing world-leading centres of clinical and research excellence to present their latest reseach findings and their potential therapeutic applications. The Conference comes at a critical point in the development of research ideas and new services relating to schizophrenia. To take place at the Swiss-Grand Hotel, Bondi, October 24-26, the program is designed to stimulate exchange of knowledge and inspirations between cutting-edge researchers, practising clinicians and interested consumers.

Australasian Schizophrenia Conference 2002

Website: www.ausc.info

NISAD'S FOUNDING TREASURER JIM BREENE RETIRES

Jim Breene's vital contribution as Secretary/Treasurer to NISAD dates back to the time when the Institute was little more than a proposal on a document. Many hundreds more corporate and financial documents were to follow; many composed by Jim, all passed under his scrutiny. Under his guidance, the Institute's foundations of charitable status, fiscal accountability, and policies and procedures were securely laid.

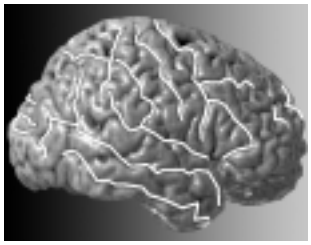
Jim's wife Carmel Breene also sat on NISAD's Board during her term as Chairperson of the Schizophrenia Fellowship of NSW - another organisation which owes much to Jim's skills.

At the Board meeting of 6 March, the Directors presented Jim with a special plaque commemorating his services to NISAD and to schizophrenia research, and wished him a long and happy retirement.

From LosAngeles to Liverpool: Mission Accomplished.

After 9 months training at the world leading UCLA Laboratory of Neuro Imaging , Paul Rasser brings the goods back to Australia.

Paul Rasser outside NISAD's Liverpool Hospital base.



One of Paul's images showing the Sucal lines used to locate the same areas on different brains.

Just by looking at pictures of brains, you might assume that they are all pretty much the same. However, the gyri (hills) and the sulci (valleys) which corrugate the surface are different in each case. This is a problem if you are trying to identify anatomical differences between healthy brains and those affected by disease. If the brains are different, anyway, how can you tell which differences are caused by the illness?

The Laboratory of Neuro Imaging (LONI) in Los Angeles solved the problem by developing a computer program which enables the sulci shown in any group of brain images to be aligned - revealing precisely where any anatomical differences occur. Dr. Paul Thompson's team at LONI is now scanning thousands of brains affected by Alzheimer's or schizophrenia to create a composite model, or 'atlas', of each disease.

Having trained with Dr. Thompson, Paul Rasser has returned to Australia with the software tools necessary to continue with the construction of the schizophrenia atlas, and is now processing brain scans supplied from NISAD's Australian centres, and from an affiliated centre in Essen, Germany.

This research is made even more valuable by combining functional (fMRI) and structural (sMRI) images. Each subject is first scanned with sMRI to provide an anatomical picture of the brain, then scanned with fMRI, while the subject completes a simple thinking task, to provide a picture of cognitive activity. Comparing the two enables any relationships between functional and anatomical abnormalities to be identified.

NISAD RECEIVES FIRST BRAIN DONATION

NISAD expressed condolences to the next of kin of Mr Frank Pool, who became the first person to complete a brain donation to the 'Gift of Hope' Tissue Donor Program (TDP) when he died in January.

Frank was seriously ill with bowel cancer at the Governor Phillip Nursing Home, Penrith, when he expressed a wish to become a brain donor. NISAD Research Assistant Lisa Azizi visited Frank to complete the TDP Consent Forms, and to interview him on his medical history. Lisa reports:

"Frank was an alert and passionate 75 year old man, who had lived a good life. His wish was to help others, so that they may have the chance to enjoy life as much as he did. He understood the importance of research and how beneficial it is for both individuals and whole communities. One of the last things he did was to arrange to have his name inscribed on the 'Welcome Wall' at the Australian Maritime Museum, which commemorates the families who have migrated to Australia over the years."

The interview information obtained on each donor's health and life-style history is what will make 'Gift of Hope' donations especially valuable as 'well characterised' brain tissue.

Over the past year, the NSW Tissue Resource Centre has provided post-mortem brain tissue from both healthy and schizophrenia-affected donors to 12 different schizophrenia research projects at 11 sites in Australia and overseas.

If you would like further information about becoming a 'Gift of Hope' donor, please call (02) 9295 8398.

Family power against schizophrenia

■ *When schizophrenia struck the Kenealy family, they decided to strike back.*

Bill and Betty Kenealy's daughter Karen was diagnosed with schizophrenia in 1985. The next five years were the usual hell associated with this illness - with Karen going in and out of psychosis, and on and off medication. In 1991, the family situation had calmed down enough for Betty to think about what she could do to help fight back against the disease. She decided to open a stall in the monthly market run by the Rotary Club of Caringbah. She had always been a talented craftworker, and thought that selling her crochet work, cane baskets, photo frames and other items might raise some money for schizophrenia-related charities. Aided by husband Bill, her craftwork stall has, since 1991, raised more than $20,000 for the Schizophrenia Fellowship of NSW, and for NISAD. Daughter Karen now lives in Toowoomba, and is coping well with the help of medication. She contributes paintings to the market stall, and says she was only able to get control of the illness through the understanding and support of her husband Stephen and parents. The next Rotary Caringbah market will be held at the Council car park, behind McDonald's, President Avenue, on Sunday 28 April. Why not drop by and say hello to Bill and Betty?

L to R: Karen Witney, Betty and Bill Kenealy, with some of the craftworks to be offered at Caringbah market.

■ *The Grahames do dinner.*

With mental illness in the family, Ann Grahame and husband William fight for more research by organising fundraising dinners for up to 24 guests at their Merewether home. NISAD supplies personalised donation slips for guests to take home. This year, two such dinners have raised over $1,500. One guest commented, "Ann presented a gourmet four course dinner. Her hospitality and calm compassionate appeal touched us all".

L toR: Grand-daughter Georgia, Bill Grahame, Ann Grahame, and George Keegan - one of 20 guests.

'Beautiful Mind' Wins Media Attention for Schizophrenia

The new Russell Crowe movie 'A Beautiful Mind' is without doubt the most powerful public awareness media event schizophrenia has ever had, and NISAD speakers have been much in demand to provide information and comment.

Orchestrated by Executive Director Jackie Crossman and leading PR firm Porter Novelli, Scientific Director Philip Ward, Director Don McDonald, and 'Gift of Hope' Patron and consumer advocate Marilyn Mitchell were interviewed by major radio stations, newspapers and magazines during the pre-premiere period.

NISAD also offered sponsor and other organisations tickets to the movie, making a commission on each one sold through bulk purchasing from Greater Union. The biggest order of 200 came from Bristol -Myers Squibb Pharmaceuticals in Melbourne. The BT Financial Group organised a great night at the movie for staff, and made a collection for NISAD in the cinema foyer.

NISAD RESEARCH

Patron: Her Excellency, Professor Marie Bashir AO, Governor of NSW

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NISAD IS FUNDED BY NSW HEALTH

Please Help to Stop Schizophrenia

As the only schizophrenia research institute in NSW, NISAD needs ongoing public support in order to continue its work. Please consider appointing NISAD as your preferred charity, and help the fight against the most devastating of all mental illnesses.

Donation: Make a donation at any time by sending a cheque; by phoning us with your credit card details, or by visiting our website at www.nisad.org.au

Pledge: Pledge to donate a set amount on a date nominated by yourself (eg. 15th of each month, or annually, etc.)

❒ **Bequest:** Remembering NISAD in your will is a gift to the future. Please tick the box if you require further information.

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Please call (02) 9295 8407 if you wish to discuss any of the options or need further information.

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NEUROSCIENCE INSTITUTE OF SCHIZOPHRENIA AND ALLIED DISORDERS

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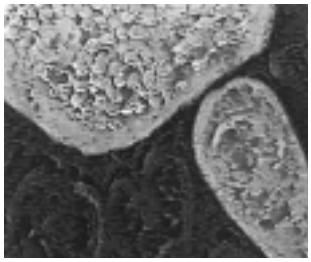
SCHIZOPHRENIA RESEARCH FROM AROUND THE WORLD

THE CASE FOR SCHIZOPHRENIA AS A DISEASE OF THE SYNAPSE

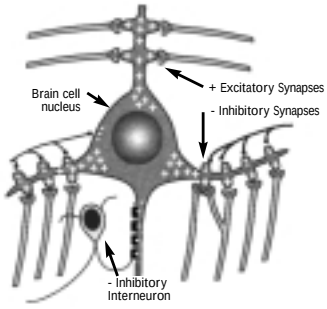
Neuroscientists at University of Pittsburgh USA are looking at damage to the synapses and the genes which may be responsible.*



Scanning electron microscope image of synapse (lower right) and a dendrite nerve channel connecting to the brain cell nucleus.

Many studies have indicated that the symptoms of schizophrenia may be caused by excessive 'pruning' of brain cells during adolescence. Now, a team of scientists at the University of Pittsburgh are focusing on the synapses, and the malfunctioning genes which could be destroying them.

To function normally, the brain must have its excitatory and inhibitory synapses working in harmony. Each and every excitatory impulse received by a neuron is automatically modified by the inhibitory system - rather like a dimmer switch on a light bulb. When this system malfunctions, or is damaged, the excitatory/inhibitory 'balance of the mind' is disturbed, and the altered signalling between brain cells may produce the chaotic thoughts, delusions, and attentional deficits of schizophrenia.



NORMAL - Before pruning

During normal childhood, an over-abundance of excitatory (+) and inhibitory (-) synapses is produced in the cerebral cortex.

SCHIZOPHRENIA - Before pruning

Because of abnormal gene functioning, less + and - signalling is produced in children who will develop schizophrenia.

NORMAL - After pruning

During normal adolescence, the number of + and - synapses is reduced, producing adult cognitive functioning and behaviour.

SCHIZOPHRENIA - After pruning

Due to lower levels of + and - signalling, synapses are over-pruned, and the symptoms of schizophrenia emerge.

The above model of the origins of schizophrenia suggests that, due to defects in gene expression, less excitatory and inhibitory signalling occurs in pre-adolescent schizophrenia brains, but that this deficit is compensated for by the natural over-abundance of synapses.

During the normal synapse pruning process of teenage years, the underlying signalling deficit triggers an over pruning of synapses, and the symptoms of schizophrenia emerge.

The recently initiated studies by NISAD's Dr Paul Tooney and Prof. Peter Schofield of the Garvan Institute will allow NISAD to utilise DNA microarray technology - enabling NSW to pursue this promising new line of schizophrenia research.

**Karoly Mirnics, Frank A. Middleton, David A. Lewis, Pat Levitt: Analysis of complex brain disorders with gene expression microarrays: schizophrenia as a disease of the synapse. University of Pittsburgh School of Medicine.*

Illustration adapted and simplified from 'Trends in Neurosciences', Vol.24 No.8 August 2001.

Visit the NISAD Website at www.nisad.org.au

HeadLines is edited, designed and produced by NISAD Marketing Director Alan Tunbridge.
The opinions expressed in HeadLines do not necessarily represent the views of all NISAD's participating scientists.

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